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41: Growth Factors 1995;12(2):99-109 Related Articles, Nucleotide, OMIM, Protein

Growth/differentiation factor-10: a new member of the transforming growth factor-beta superfamily related to bone morphogenetic protein-10

Cunningham NS, Jenkins NA, Gilbert DJ, Copeland NG, Reddi AH, L

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We have identified a new member of the transforming growth factor-beta (TGF-beta) superfamily, growth/differentiation factor-10 (GDF-10), which is highly related to morphogenetic protein-3 (BMP-3). The nucleotide sequence of GDF-10 encodes a predicted protein of 476 amino acids with a molecular weight of approximately 55 kDa. The GDF-10 polypeptide contains a potential signal sequence for secretion, a consensus RXXR proteolytic processing site, and a carboxy-terminal domain with considerable homology to other known members of the TGF-beta superfamily. In the major domain, GDF-10 is more homologous to BMP-3 (83% amino acid identity) than to any other previously identified TGF-beta family member. GDF-10 shows significant homology to BMP-3 (approximately 30% amino acid sequence identity) in the pro- region of the molecule. Based on these sequence comparisons, GDF-10 and BMP-3 define a new subgroup within the larger TGF-beta superfamily. Northern analysis, GDF-10 mRNA was detected primarily in murine uterus, testis, and brain and to a lesser extent in liver and spleen. In addition, GDF-10 was present in both neonatal and adult bone samples, with higher levels being detected in the calvaria than in long bone. These results suggest that GDF-10 may play multiple roles in regulating cell differentiation events, including those involved in skeletal morphogenesis. Gdf10 was mapped to the proximal region of mouse chromosome 14 closely linked to a gene known to contain a spontaneous recessive mutation that is associated with a skeletal defect.

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PMID: 8679252 [PubMed - indexed for MEDLINE]

42: Nature 1994 Apr 14;368(6472):639-43

Comment in:

- Nature. 1994 Apr 14;368(6472):587-8

Limb alterations in brachypodism mice due to mutations in a member of the TGF beta-superfamily.

Storm EE, Huynh TV, Copeland NG, Jenkins NA, Kingsley DM, Lee S

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The mutation brachypodism (bp) alters the length and number of bones in the limbs of mice but spares the axial skeleton. It illustrates the importance of specific genes controlling the morphogenesis of individual skeletal elements in the tetrapod. We now report the isolation of three new members of the transforming growth factor (TGF-beta) superfamily (growth/differentiation factors (GDF) 5, 6 and 7) and their mapping, expression patterns and sequencing that mutations in Gdf5 are responsible for the skeletal alterations in bp mice. GDF5 and the closely related GDF6 and GDF7 form a new subgroup of factors related to known bone- and cartilage-inducing molecules, the bone morphogenetic proteins (BMPs). Studies of Bmp5 mutations in short ear mice have shown that at least one other BMP gene is also required for normal skeletal development. The highly specific skeletal alterations in bp and short ear mice suggest that members of the BMP family control the formation of different morphologies of the mammalian skeleton.

PMID: 8145850 [PubMed - indexed for MEDLINE]

☐ **43:** Prog Growth Factor Res 1994;5(1):99-118 Related Articles, Genome, Nucleotide

Erratum in:

- Prog Growth Factor Res 1994;5(2):following 261

Evolution of the transforming growth factor-beta superfamily.

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Transforming growth factor beta 1 (TGF-beta 1) is the prototype of an increasingly complex superfamily of growth and differentiation factors. To date, a total of 23 beta-like sequences have been published, probably representing 23 distinct genes. These sequences were obtained from mammalian, avian, amphibian and insect species, emphasising the ancient nature of the TGF-beta superfamily peptides. This review summarises current hypotheses concerning the evolutionary history of this superfamily, based on the molecular phylogeny of the published sequences. Analysis of the deduced amino acid sequences leads to the definition of five main groups within the superfamily (TGF-beta, Bone Morphogenetic Proteins [BMP], Anti-Mu

Hormone [AMH], Inhibin alpha [INH alpha] and GDF-9) and six subgroup BMPs (60A, Decapentaplegic [dpp], Vg1, BMP-3, Inhibin beta [INH beta / nodal). This classification predicts possible phylogenetic and functional relationships among these proteins.

PMID: 8199356 [PubMed - indexed for MEDLINE]

☐ 44: Mol Endocrinol 1990 Jul;4(7):1034-40

Related Articles, Nucleotide, OMIM

Identification of a novel member (GDF-1) of the transforming factor-beta superfamily.

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A cDNA clone encoding a new member (designated GDF-1) of the transforming factor-beta (TGF beta) superfamily was isolated from a library prepared from mouse embryos. The nucleotide sequence of GDF-1 predicts a protein of 355 acids with a mol wt of 38,600. The sequence contains a pair of arginine residues at positions 236-237, which is likely to represent a site for proteolytic processing. The terminus following the presumed dibasic cleavage site shows significant homology with all of the known members of the TGF beta superfamily, matching the other family members at all of the invariant positions, including the seven cysteine residues with their characteristic spacing. GDF-1 is most homologous to *Xenopus* Vg-1 (52%) and is likely to be the murine homolog of Vg-1. In vitro translation experiments with GDF-1 being a secreted glycoprotein. Genomic Southern analysis indicates that GDF-1 may be highly conserved across species. These results suggest that GDF-1 is most likely an extracellular factor mediating cell differentiation events during development.

PMID: 1704486 [PubMed - indexed for MEDLINE]

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